

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number
WO 2005/060946 A1

(51) International Patent Classification⁷: A61K 31/00,
31/427, 31/425, 31/4015, 31/4025, 31/566, A61P 19/10

(21) International Application Number:
PCT/IB2004/004049

(22) International Filing Date: 6 December 2004 (06.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/530,839 17 December 2003 (17.12.2003) US

(71) Applicant (for all designated States except US): PFIZER
PRODUCTS INC. [US/US]; Eastern Point Road, Groton,
CT 06340 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): KE, Hua, Zhu
[US/US]; Pfizer Global Research & Development, Eastern
Point Road, Groton, CT 06340 (US). THOMPSON,
David, Duane [US/US]; Pfizer Global Research & Devel-
opment, Eastern Point Road, Groton, CT 06340 (US).

(74) Agent: FULLER, Grover, F., Jr.; c/o LAWRENCE,
Jackie, Pfizer Inc. MS8260-1615, Eastern Point Road,
Groton, CT 06340 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: CONTINUOUS COMBINATION THERAPY WITH SELECTIVE PROSTAGLANDIN EP₄ RECEPTOR AGONISTS
AND AN ESTROGEN FOR THE TREATMENT OF CONDITIONS THAT PRESENT WITH LOW BONE MASS

(57) Abstract: This invention is directed to methods for treating conditions which present with low bone mass in a patient in need thereof using continuous combination therapy with a synergistically effective combination of an EP₄ receptor selective agonist or a pharmaceutically acceptable salt thereof, such as 5-(3-{2S-[3R-hydroxy4-(3-trifluoromethyl-phenyl)-butyl]-5-oxo-pyrrolidin-1-yl}-propyl)-thiophene-2-carboxylic acid or a pharmaceutically acceptable salt thereof; and an estrogen or a pharmaceutically effective salt thereof. The present methods are useful for treating conditions that present with low bone mass including osteoporosis, osteotomy, osteoporotic fracture, childhood idiopathic bone loss, periodontitis and low bone mass and for enhancing bone healing following facial reconstruction, maxillary reconstruction or mandibular reconstruction, inducing vertebral synostosis, enhancing long bone extension, enhancing the healing rate of a bone graft or a long bone fracture or enhancing prosthetic ingrowth in a patient in need thereof.



WO 2005/060946 A1